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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/823,772 | 03/30/2001 | Beat Mollet | 88265-4011 | 6428 |

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06/19/2003

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EXAMINER

HUTSON, RICHARD G

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 06/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicant(s)

09/823,772

Applicant(s)

MOLLET ET AL.

Examiner

Richard G Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 April 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,5-8 and 15-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,5-8 and 15-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>13</u> . | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Applicants amendment of the specification, and claims 1, cancellation of claims 3, 4, 9-14 and the addition of new claims 15-20, Paper No. 12, 4/14/2003, is acknowledged. Claims 1, 2, 5-8 and 15-20 are at issue and are present for examination. Applicants' arguments filed on 4/14/2003, Paper No. 12, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Priority

As stated in the previous office action, Applicants statement that this application is a continuation of the U.S. national stage designation of International Application PCT/EP99/06818 filed September 15, 1999, the content of which is expressly incorporated herein by reference thereto is acknowledged, however, it is noted that this application is a continuation of International Application PCT/EP99/06818, filed September 15, 1999, which designates the United States. Applicants traversal of this is not found persuasive. This application is not a continuation of the U.S. national stage of the international application. The U.S. national stage of the international application is a 371 application, which is an application in and of itself. This application is not a continuation of a U.S. national stage application (371), but as stated above and previously this application is a continuation of the International Application PCT/EP99/06818, filed September 15, 1999, which designates the United States. If it

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remains applicants intent that this is a continuation of the U.S. national stage designation of International Application PCT/EP99/06818 filed September 15, 1999, it is requested that applicants supply the application number of the national stage (371) of PCT/EP99/06818 , from which applicants claim this is a continuation of.

Information Disclosure Statement

Applicants filing of information disclosures, filed 3/3/2001, and Paper No. 13, filed 4/14/2003, are acknowledged. Those references considered have been initialed.

Drawings

The drawings filed on 3/30/2001 are previously objected to for the reasons stated on the enclosed form PTO-948. Note, applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a). The referred to drawings which applicants state were filed with the previous amendment were not found with the amendment.

Specification

The disclosure is objected to because of the following informalities:

As stated above under the priority section, this application is a continuation of International Application PCT/EP99/06818 filed September 15, 1999, not the national stage designation of this application as stated above.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 5-8, 15-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 15 (16-20 dependent on) are indefinite in that the recitation "...substantial amounts of iso-valeric acids..." is unclear. What is a substantial amount of isovaleric acid? Applicants argue that one skilled in the art would readily appreciate what is meant by "...substantial amounts of isovaleric acids..." and thus the claim is definite. This argument is not found persuasive and in response to applicants statement that that one skilled in the art would readily appreciate what is meant by "...substantial amounts of isovaleric acids...", applicants are asked, then what amount of isovaleric acid would one of skill in the art would appreciate as being a "...substantial amounts of isovaleric acids..."

The rejection of claim 2 as being indefinite the recitation "...taste perceptible amounts of iso-valeric acids" is hereby withdrawn. As acknowledged by applicants, taste is specific to the person that is tasting, and different individuals are able to taste differently. This limitation is interpreted as broad as reasonably possible in that it means any amount that any person tasting is able to perceive.

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Claim 1, 2, 5-8 are indefinite in that the recitation "...the *ywfL* gene" is unclear. This rejection is similar to the previous rejection of claim 4 under 112 2nd paragraph which was made against "modified gene(s) is derived from the *ywfL* gene". Applicants argued the previous rejection as it applies to this rejection on the basis that the sequence of the *ywfL* gene is already known in the state of the art and that a corresponding reference has been indicated in the specification. The reference to which applicants refer is Kunst et al. "The complete genome sequence of the gram positive bacterium *B. subtilis*", Nature 390 (1997), 249-256. Applicants argument which is based on the sequence of the *ywfL* gene is already known and the presentation of the complete genome of *B. subtilis* is not found persuasive, because while the sequence of the complete genome of *B. subtilis* is known and the complete genome encompasses the *ywfL* gene, it remains to be seen that "e sequence of the *ywfL* gene is known". Especially as much as this is used to define applicants intent of what is encompassed by the "*ywfL* gene".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to claims 1-6 and 8. In response applicants have cancelled claims 3 and 4 and amended claim 1 and argue this rejection on the basis of applicants amendment.

Applicants argue that based on applicants amendment that they have overcome this rejection on the basis that the claimed bacterial strains contain the *ywfI* gene and there is enough identifying features for the strains and the rejection has been rendered moot. Further applicants assert that in response to earlier comments that no additional gene or any modifications thereof beyond the *ywfI* gene and its deletion was described has been rendered moot, because applicants have amended claim 1 to explicitly recite the *ywfI* gene and its deletion. Applicants amendments and supporting argument is not found persuasive because while applicants state that they have amended claim 1 to recite "the *ywfI* gene and its deletion." The actual amendment recites "...a *ywfI* gene product involved in the biosynthesis of iso-valeric acids, which gene product has been deleted or **is essentially non-functional**..." Applicants have not described any of the claimed modifications of the *ywfI* gene product beyond its deletion. Applicants have not described any of the potential modifications of the *ywfI* gene product that result in making the *ywfI* gene product essentially non-functional.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

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Claims 1-6 and 8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *B. subtilis* strain, wherein the *ywfL* gene has been deleted, such that the strain cannot produce substantial amounts of isovaleric acid, does not reasonably provide enablement for any bacterial strain of the *B. subtilis* group, wherein the *ywfL* gene is essentially non-functional such that the strain cannot produce substantial amounts of isovaleric acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to claims 1-6 and 8. In response applicants have cancelled claims 3 and 4 and amended claim 1 and argue this rejection on the basis of applicants amendment.

Applicants argue that modification of a *ywfI* gene product to render it essentially non-functional is also enabled since the modification would have the same effect as deleting the *ywfI* gene product. Applicants submit that as explained in the present specification, the gene products, preferably a *ywfI* gene product, may comprise polypeptides acting as enzymes within the synthesis pathway or acting as regulatory agents for the production of iso-valeric acids and that the *ywfI* gene may be deleted from the genome or modified such that the gene is not transcribed into a functional product. Herein lies the basis of the current enablement rejection. While applicants have taught the claimed *Bacillus* strain in which the *ywfI* gene has been deleted, applicants have not taught nor given guidance as to how one modify the *ywfI* gene product such that it would be rendered essentially non-functional.

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As discussed in the previous office action, the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a *B. subtilis* strain, wherein the *ywfL* gene has been deleted, such that the strain cannot produce substantial amounts of isovaleric acid.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those bacterial strains having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 7 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection was stated in the previous office action as it applied to claim 7, however applicants did not respond to the rejection and thus it is repeated below.

The invention of claim 7 is appears to be drawn to a novel *B. subtilis* strain I-2077. Since the *B. subtilis* strain I-2077 is the invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The organism is not fully disclosed, nor has it been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the *B. subtilis* strain I-2077 in accordance with 37 CFR 1.801-1.809.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

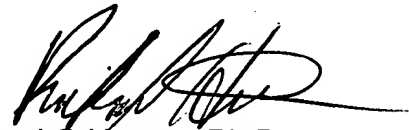
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

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June 18, 2003